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ATTORNEY'S DOCKET NUMBER: 0492611-0505

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Chau *et al.* Examiner: Rogers, J.W.
Serial No: 10/668,045 Art Unit: 1618
Filing Date: September 22, 2003
Title: Polymer-Linker-Drug Conjugates for Targeted Drug Delivery

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

TRANSMITTAL LETTER

Enclosed are the following documents:

1. Statement under 37 C.F.R. §§ 1.56, 1.97, and 1.98 (6 pages);
2. Form PTO-1449 (3 pages);
3. Cited Art (18 references);
4. Return Postcard; and
5. Credit Card Payment Form

Respectfully submitted,

Charles E. Lyon, D. Phil.
Registration No. 56,630

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Two International Place
Boston, MA 02110
t (617) 248-5000
f (617) 248-4000

Dated: October 31, 2006

Certificate of Mailing

I certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

October 31, 2006

Date

Signature

Nicole A. Dozier

Typed or Printed Name of person signing certificate




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CERTIFICATE OF MAILING

I hereby certify that the foregoing document is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on October 31, 2006.


Name: Nicole A. Dozier

Sir:

INFORMATION DISCLOSURE STATEMENT

Pursuant to the duty of disclosure under 37 CFR §§ 1.56, 1.97 and 1.98, Applicant requests consideration of this Information Disclosure Statement.

Type of Statement

The present Information Disclosure Statement is:

- ☐ An *original* Information Disclosure Statement; or
☒ A *supplemental* Information Disclosure Statement.

11/06/2006 CNGUYEN 00000009 10660045

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Compliance with 37 CFR § 1.97

The present Information Disclosure Statement is being filed:

- ☐ Pursuant to 37 CFR § 1.97(b); no fee or certification is required:
 - ☐ Within three months of the filing date of a national application other than a continued prosecution application under § 1.53(d);
 - ☐ Within three months of the date of entry of the national stage as set forth in § 1.491 in an international application;
 - ☐ Before the mailing of a first Office action on the merits; or
 - ☐ Before the mailing of a first Office action after the filing of a request for continued examination under § 1.114.
- ☒ Pursuant to 37 CFR § 1.97(c) after the dates listed above but before the mailing date of any of a final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application; Applicant hereby *either*:
 - ☒ Certifies that *either*:
 - ☐ each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement; or
 - ☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making

reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of

the information disclosure statement; or

☒ Includes herewith the fee set forth in § 1.17(p),

☐ Pursuant to 37 CFR § 1.97(d), after the mailing date of any final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application; Applicant hereby *both*:

☐ Certifies that *either*:

☐ each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement; or

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of

the information disclosure statement; and

☐ Includes herewith the fee set forth in § 1.17(p).

Content of the Information Disclosure Statement

Applicant hereby makes of record in the above-identified application the reference(s) listed on the attached form PTO-1449 (modified). The order of presentation of the references should not be construed as an indication of the importance of the references.

Applicant includes copies of references as indicated below:

- ☐ A copy of each cited reference not indicated with an asterisk is included, except for U.S. patents and published U.S. patent applications for which the submission requirements has been waived by the PTO in the Official Gazette Notice of August 5, 2003, for applications filed after June 30, 2003;
- ☒ A copy of each of the references cited on the attached form PTO-1449 (modified) is enclosed, except for U.S. patents and published U.S. patent applications for which the submission requirement has been waived by the PTO in the Official Gazette Notice of August 5, 2003, for applications filed after June 30, 2003;
- ☐ Copies of references indicated with an asterisk on the attached form PTO-1449 are not included pursuant to 37 CFR § 1.98(d) because they were previously provided to the United States Patent Office in an Information Disclosure Statement that complies with 37 CFR § 1.98(a)-(c) and was submitted in the following patent application that is relied upon in the present case for an earlier effective filing date under 35 USC § 120:

Serial Number	Filing Date	Status

- ☐ Copies of English translations of one or more non-English references are included.

Applicant hereby makes the following additional information of record in the above-identified application:

Applicant certifies that the Information Disclosure Statement *either*:

- ☒ Does not contain non-English language citations;
- ☐ Includes one or more translations of a non-English citation; or
- ☐ Does contain non-English language citations

Remarks

The submission of this Information Disclosure Statement should not be construed as a representation that a search has been made.

The submission of this Information Disclosure Statement shall not be construed to be an admission that the information cited in the statement is, or is considered to be, material to patentability as defined in § 1.56(b) .

The submission of this Information Disclosure Statement shall not be construed as a representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 USC §102.

It is respectfully requested that:

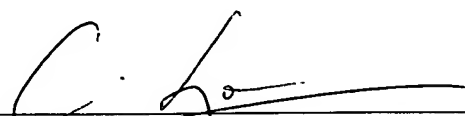
1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;
2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited patent(s) and publication(s) has (have) been fully considered by the Patent and Trademark Office during the examination of this application; and

3. The citations for the patent(s) and publication(s) be printed on any patent which issues from this application.

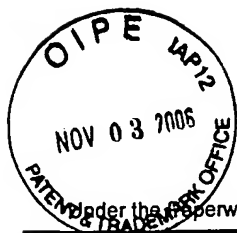
Notwithstanding any statements by Applicants, the Examiner is urged to form his or her own conclusions regarding the relevance of the cited reference(s).

Respectfully submitted,

Dated: October 31, 2006


Charles E. Lyon, D. Phil.
Registration No. 56,630

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PTO/SB/08A (07-06)

Approved for use through 09/30/2006. OMB 0651-0031

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Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	10/668,045
				Filing Date	September 22, 2003
				First Named Inventor	Chau <i>et al.</i>
				Art Unit	1618
Examiner Name	Rogers, J.W.				
Attorney Docket Number	0492611-0505 (MIT 9991)				
Sheet	1	Of	1		

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-6,372,205	April 16, 2002	Duncan <i>et al.</i>	

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No. ¹	Foreign Patent Document Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶

Examiner Signature		Date Considered	
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹Applicant's unique citation designation number (optional). ²See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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			Examiner Name	Rogers, J.W.	
Sheet	1	Of	2	Attorney Docket Number	0492611-0505 (MIT 9991)

NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No. ¹	Include the name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Chau <i>et al.</i> , "Antitumor efficacy of a novel polymer-peptide-drug conjugate in human tumor xenograft models", <i>Int. J. Cancer</i> , 118 :1519-1526, , 2006.	
		Chau <i>et al.</i> , "Synthesis and characterization of dextran-peptide-methotrexate conjugates for tumor targeting via mediation by matrix metalloproteinase II and matrix metalloproteinase IX", <i>Bioconjugate Chem.</i> , 15 : 931-941, 2004.	
		Corticchiato <i>et al.</i> , "Cystatin-C and cathepsin-B in human colon-carcinoma-expression by cell-lines and matrix degradation", <i>Int. J. Cancer</i> , 52 : 645-652, 1992.	
		Duncan <i>et al.</i> , "Preclinical evaluation of polymer-bound doxorubicin", <i>J. Controlled Release</i> , 19 : 331-346, 1992.	
		Duncan <i>et al.</i> , "Polymer-drug conjugates, PDEPT and PELT: basic principles for design and transfer from the laboratory to the clinic", <i>J. Controlled Release</i> , 74 :135-146, 2001.	
		Duncan <i>et al.</i> , "Polymer-drug conjugates: towards a novel approach for the treatment of endocrine-related cancer", <i>Endocrine-Related Cancer</i> , 12 :S189-S199, 2005.	
		Hopewell <i>et al.</i> , "Preclinical evaluation of the cardiotoxicity of PK2: a novel HPMA copolymer-doxorubicin-galactosamine conjugate antitumour agent", <i>Hum. Exp. Toxicol.</i> , 20 : 461-470, 2001.	
		Jane <i>et al.</i> , "Cathepsin B localizes to plasma membrane caveolae of differentiating myoblasts and is secreted in an active form at physiological pH", <i>Biol. Chem.</i> , 387 : 223-234, 2006.	
		Khalfan, "Study of thiol proteases of normal human skin fibroblasts", <i>Cell Biochemistry and Function</i> , 9 :55-62, 1991.	
		Linebaugh <i>et al.</i> , "Exocytosis of active cathepsin B enzyme activity at pH 7.0, inhibition and molecular mass" <i>Eur. J. Biochem.</i> , 264 :100-109, 1999.	
		Loadman <i>et al.</i> , "Pharmacokinetics of PK1 and doxorubicin in experimental colon tumor models with differing responses to PK1", <i>Clin. Cancer Res.</i> , 5 :3682-3688, 1999.	

		Moin <i>et al.</i> , "Tumor cell membrane cathepsin B", <i>Biol. Chem.</i> , 379:1093-1099, 1998.	
		Noguchi <i>et al.</i> , "Early phase tumor accumulation of macromolecules: a great difference in clearance rate between tumor and normal tissues", <i>Jpn. J. Cancer Res.</i> , 89:307-314, 1998.	
		Ruzza <i>et al.</i> , "Fluorescent, internally quenched, peptides for exploring the pH-dependent substrate specificity of cathepsin B" <i>J. Pept. Sci.</i> , 12:455-461, 2006.	
		Seymour <i>et al.</i> , "The pharmacokinetics of polymer-bound adriamycin", <i>Biochem. Pharmacol.</i> , 39:1125-1131, 1990.	
		Seymour <i>et al.</i> , "Tumour tropism and anti-cancer efficacy of polymer-based doxorubicin prodrugs in the treatment of subcutaneous murine B16F10 melanoma", <i>British J. Cancer</i> , 70:636-641, 1994.	
		Song <i>et al.</i> , "The active-site residue Cys-29 is responsible for the neutral-pH inactivation and the refolding barrier of human cathepsin B", <i>FEBS Lett.</i> , 475:157-162, 2000.	
		Vasey <i>et al.</i> , "Phase I clinical and pharmacokinetic study of PK1 [N-(2-hydroxypropyl)methacrylamide copolymer doxorubicin]: first member of a new class of chemotherapeutic agents-drug-polymer conjugates", <i>Clin. Cancer Res.</i> , 5: 83-94, 1999.	

Examiner Signature		Date Considered	
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

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